

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
 BENJAMIN L. VOLK
 THOMPSON COBURN LLP
 ONE US BANK PLAZA
 ST. LOUIS, MO 63101

PCT

NOTIFICATION OF TRANSMITTAL OF
 THE INTERNATIONAL SEARCH REPORT AND
 THE WRITTEN OPINION OF THE INTERNATIONAL
 SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

		Date of mailing (day/month/year) 25 JUL 2008
Applicant's or agent's file reference 53-047-70498		FOR FURTHER ACTION See paragraphs 1 and 4 below
International application No. PCT/US07/75723		International filing date (day/month/year) 10 August 2007 (10.08.2007)
Applicant WASHINGTON UNIVERSITY		

1. The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes 1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 338.82.70.

For more detailed instructions, see the notes on the accompanying sheet.

2. The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
 no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

Shortly after the expiration of 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise, the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer Shubo (Joe) Zhou  Telephone No. (571)-272-1600
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(See notes on accompanying sheet)

Form PCT/ISA/220 (January 2004)

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Thompson Coburn LLP **THOMPSON COBURN**

PATENT COOPERATION TREATY

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 53-047-70498	FOR FURTHER ACTION	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US07/75723	International filing date (day/month/year) 10 August 2007 (10.08.2007)	(Earliest) Priority Date (day/month/year) 10 August 2006 (10.08.2006)
Applicant WASHINGTON UNIVERSITY		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 2 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the Report**

a. With regard to the **language**, the international search was carried out on the basis of:

the international application in the language in which it was filed.

a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 Rule 43.6 *bis(a)*

c. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. **Certain claims were found unsearchable** (See Box No. II)

3. **Unity of invention is lacking** (See Box No. III)

4. With regard to the title,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

5. With regard to the abstract,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

a. the figure of the drawings to be published with the abstract is Figure No. _____

as suggested by the applicant.

as selected by this Authority, because the applicant failed to suggest a figure.

as selected by this Authority, because this figure better characterizes the invention.

b. none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

IPC: G01N 33/48(2006.01)
G01N 33/48(2006.01)

USPC: 702/19,20

According to International Patent Classification (IPC) or to both national classification

Check these
refs & edit
restart CCR
remove NPI

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 702/19, 20

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EDGAR, R.C. MUSCLE: Multiple Sequence Alignment with High Accuracy and High Throughput. Nucleic Acids Research, 2004, Vol. 32, No. 5, pages 1792-1797, entire document.	1-99
A	THOMPSON et al. The CLUSTAL_X Windows Interface:Flexible Strategies for Multiple Sequence Alignment Aided by Quality Analysis Tools. Nucleic Acids Research, 1997, Vol. 25, No. 24, pages 4876-4882, entire document.	1-99
A	CHENNA et al. Multiple Sequence Alignment with the Clustal Series of Programs. Nucleic Acids Research, 2003, Vol. 31, No. 13, pages 3497-3500, entire document.	1-99
A	JEANMOUGIN et al. Multiple Sequence Alignment with Clustal X. TIBS, 1998, Vol. 23, pages 403-405, entire document.	1-99
A	ALTSCHUL et al. Basic Local Alignment Search Tool. Nucleic Acids Research, 2003, Vol. 31, No. 13, pages 3497-3500, entire document.	1-99

<input type="checkbox"/>	Further documents are listed in the continuation of Box C.	<input type="checkbox"/>	See patent family annex.
* Special categories of cited documents:			
"A"	document defining the general state of the art which is not considered to be of particular relevance	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E"	earlier application or patent published on or after the international filing date	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

23 June 2008 (23.06.2008)

Date of mailing of the international search report

25 JUL 2008

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (571) 273-3201

Authorized officer

Shubo (Joe) Zhou

Telephone No. (571)-272-1600

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
BENJAMIN L. VOLK
THOMPSON COBURN LLP
ONE US BANK PLAZA
ST. LOUIS, MO 63101

PCT

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

(PCT Rule 43bis.1)

		Date of mailing (day/month/year)	25 JUL 2008
Applicant's or agent's file reference 53-047-70498		FOR FURTHER ACTION See paragraph 2 below	
International application No.	International filing date (day/month/year)	Priority date (day/month/year)	
PCT/US07/75723	10 August 2007 (10.08.2007)	10 August 2006 (10.08.2006)	
International Patent Classification (IPC) or both national classification and IPC IPC: G01N 33/48(2006.01) G01N 33/48(2006.01) USPC: 702/19,20			
Applicant WASHINGTON UNIVERSITY			

1. This opinion contains indications relating to the following items:

<input checked="" type="checkbox"/>	Box No. I	Basis of the opinion
<input type="checkbox"/>	Box No. II	Priority
<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
<input type="checkbox"/>	Box No. IV	Lack of unity of invention
<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
<input type="checkbox"/>	Box No. VI	Certain documents cited
<input type="checkbox"/>	Box No. VII	Certain defects in the international application
<input type="checkbox"/>	Box No. VIII	Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Date of completion of this opinion 23 June 2008 (23.06.2008)	Authorized officer Shubo (Joe) Zhou Telephone No. (571)-272-1600
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Form PCT/ISA/237 (cover sheet) (April 2007)

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Thompson Coburn LLP

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US07/75723

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

the international application in the language in which it was filed
 a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of:

a. type of material

a sequence listing
 table(s) related to the sequence listing

b. format of material

on paper
 in electronic form

c. time of filing/furnishing

contained in the international application as filed.
 filed together with the international application in electronic form.
 furnished subsequently to this Authority for the purposes of search.

4. In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US07/75723

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>1-99</u>	YES
	Claims <u>NONE</u>	NO
Inventive step (IS)	Claims <u>1-99</u>	YES
	Claims <u>NONE</u>	NO
Industrial applicability (IA)	Claims <u>1-99</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-99 meet the criteria set out in PCT Article 33(2)-(3) because the prior art does not teach or fairly suggest the claimed method and apparatus for sequence alignment searching, the apparatus comprising: a first stage configured to (1) receive a bit stream that is representative of a database sequence and (2) process the bit stream to produce a plurality of seeds, each seed being indicative of a similarity between a substring of the database sequence and a substring of a query sequence; a second stage configured to perform an ungapped extension analysis on the seeds generated by the first stage, thereb generating a plurality of high scoring pairs (HSPs); and a third stage configured to perform a gapped extension analysis on the HSPs generated by the second stage, thereby determining whether any HSPs exist that will produce alignment of interest between the database sequence and the query sequence; and wherein the first stage, the second stage, and at least a portion of the third stage are implemented as a data processing pipeline on at least one hardware logic device.

Claims 1-99 meet the criteria set out in PCT Article 33(4) because the claimed method is useful in pharmaceutical and/or medical industry for identifying biomarkers (nucleic acid and proteins) for diagnosis and/or treatment, and useful as a research tool in the industries.